

REMARKS

Claims 1-15 are pending. Claims 1 and 12 have been amended in order to more clearly define the invention. No new matter has been added.

Rejection under 35 USC 112 second paragraph

Claim 12 has been rejected under 35 USC 112 as indefinite. Applicants respectfully traverse. Steps (i) and (j) are not the same. The salt prepared by step (i) is determined by the choice of anion A- used in step (g). For instance in Example 9, A- is benzoate as that salt provides the greatest yield and purity. However the salt prepared by step (j) is determined by the choice of anion X- used in step (j). This choice is determined by different criteria such as stability and formulatability. In the an embodiment. For instance, in Example 10) anion X- is maleate.

Rejection under 35 USC 103

Claims 1-15 are rejected under 35 USC 103(a) and unpatentable over Milecki and US6,878,721 and US6,800,643.

Applicants respectfully traverse. The examiner has not established a prima facie case of obviousness. To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, all words in a claim must be considered in judging the patentability of that claim against the prior art." (See MPEP §2143). In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974), requires that each claim feature must be present (i.e., taught or suggested) by an asserted combination. KSR Int'l Co. v. Teleflex Inc., et al., 127 S. Ct. 1727 (2007), did not overrule In re Royka. The KSR decision did not address the issue of the all elements test because all of the elements were present in the asserted combination. New, revised §2143.03 instructs examiners to consider each claim feature. However, in addition to such consideration, In re Royka still requires that each claim feature must be present by an asserted combination.

Initially, with regard to Milecki, Applicants note that this reference is misplaced and improper as there is no disclosure of the instant compound of formula I nor a process for preparing compounds of formula I. The present claims are directed to a process for preparing 5-(alpha-haloacetyl)-8-substituted oxy-(1*H*)-quinolin-2-ones in high selectivity and yield that is suitable for industrial scale manufacture. The process minimizes or eliminates the formation of regioisomers, such as 7-acetyl-8-benzyloxy-(1*H*)-quinolin-2-one-(1*H*).

Milecki et al discloses derivatives of 8-hydroxy-5-[2-[(1-phenyl-2-methylprop-2-yl)amino]-1-hydroxyethyl]carbostyrl (compounds 10-13) with beta-adrenergic properties. Scheme I discloses how such compounds are prepared at a laboratory scale. Milecki does not disclose 5-(alpha-haloacetyl)-8-substituted oxy-(1*H*)-quinolin-2-one or a method for preparing same. In fact Milecki does not disclose step (a), (b) or (c) of the invention as claimed in claim 1. Thus, There is no reason for one skilled in the art who is faced with the technical problem of preparing 5-(alpha-haloacetyl)-8-substituted oxy-(1*H*)-quinolin-2-ones in high selectivity and yield that is suitable for industrial scale manufacture, to look to Milecki to solve that problem.

US 6878721 discloses ethanolamine derivatives that are active beta-2 adrenoceptor agonists. One such compound is 5-[(R)-2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-(1*H*)-quinolin-2-one. Example 1 states that compound is prepared using the procedure disclosed in US 5750701, which involves reacting 5-acetyl-8-benzyloxy-carbostyrl with the halogenating agent benzyltrimethylammonium dichloro-iodate in the presence of solvents 1,2-dichloroethane and methanol but does not disclose how 5-acetyl-8-benzyloxy-carbostyrl is prepared. US 6878721 does not fix the deficiency of Milecki. Thus, US 6878721 alone or in combination with Milecki does not help the skilled person to solve the problem of preparing 5-(alpha-haloacetyl)-8-substituted oxy-(1*H*)-quinolin-2-ones, especially for industrial scale manufacture.

US 6800643 discloses combination products containing a 5-[(R)-2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-(1*H*)-quinolin-2-one salt and a steroid. This reference alone or in combination with Milecki and 6878721 does not teach or suggest how to prepare 5-(alpha-haloacetyl)-8-substituted oxy-(1*H*)-quinolin-2-ones. Therefore US 6800643 is no more useful than US 6878721 in helping the skilled person to solve the problem of preparing 5-(alpha-haloacetyl)-8-substituted oxy-(1*H*)-quinolin-2-ones, especially for industrial scale manufacture.

The cited references either alone or in combination do not disclose all of the elements of the claimed invention. Thus, Applicants respectfully asserts that the references cited by the Examiner, singularly or in combination, fail to teach the process of claims 1-15. Therefore, the process of claims 1-15 are not obvious over Milecki when combined with US 6878721 and US 6800643.

In view of the above, Applicants believe that the pending claims 1-15 are in condition for allowance and respectfully request that the rejection of claims 1-15 be reconsidered and withdrawn. If any issues remain, the Examiner is invited to telephone the undersigned.

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A handwritten signature in cursive script, appearing to read "Milagros A. Cepeda", written in dark ink.

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